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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,538	05/03/2001	Brita Schulze	047664-5002-US	4013

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EXAMINER	
SHARAREH, SHAHNAM J	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 03/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/847,538	SCHULZE ET AL.	
	Examiner	Art Unit	
	Shahnam Sharareh	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6/3/2005, 12/27/2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33,37-51 and 53-74* is/are pending in the application.

4a) Of the above claim(s) *33,37-51,53-57,62,64-66 and ~~68-73~~* 68 and 70-73 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *58-61,63,67,69 and 74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 03, 2005 has been entered.

Claims 33, 37-51, 53-74 are pending. Claims 37-51,70-73 were subject to a Restriction Requirement and stand withdrawn because they are not directed to elected invention. Claims 70-73 are withdrawn because they are not directed to elected species. (see Office Actions filed on January 12 2005 and July 16, 2003). Claims 33, 53-69, 74 were further subject to a Restriction Requirement issued on August 26, 2005.

In response filed December 25, 2007, applicant has elected with traverse Group II, claims 58-61, 63, 65, 67, 69, 74, and the species of taxane as the therapeutic agent. Said election is being acknowledged. Applicant's traversal is on the grounds that both Groups I and II are directed to similar steps and reagents thus they should be examined together. This argument is not found persuasive because the standard for Restriction Requirement is not whether claims employ similar steps or reagents. Rather, the standard is based on whether each set of claims is capable of supporting different patenable inventions. (see MPEP 806-808). Since the restricted claims are patentably distinct for the reasons of record, the Requirement is proper.

Claims 33, 37-51, 53-57, 62, 64-65, 66, 69-73 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention or species, there being no allowable generic or linking claim.

Claims 58-61, 63, 67, 69, 74 are now being examined on their merits to the extent that they read on the elected species.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 58-61, 63, 67, 69, 74 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 51-59 of copending Application No. 10/519,193 and claims 1-15 of copending Application No. 11/018574. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are directed to overlapping inventions.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The instant application is directed to methods of modifying a therapeutic agent comprising associating the agent with one or more cationic component to produce a composition having optimal range of zeta potential and dispersing the composition in a medium to form colloids having a size of about 10 nm to about 400 nm, wherein the composition exhibits a specific zeta potential and comprise liposomal moieties.

Both sets of copending applications are directed to methods of producing a liposomal preparation comprising a therapeutic agent such as a taxane derivative and a cationic lipid, wherein the liposomes particle size ranges between 50nm to 400nm.

The instant claims only differ in reciting the desired zeta potential. However such properties can be optimized by routine experimentation to maximize efficacy of the therapeutic agent. Accordingly, it would have been obvious to one of ordinary skill in the art at the time of invention to practice the scope of the instant claims when in possession of the claims in the copending applicaiton.

Claim Objections

Claims 58-61, 63, 67, 69, 74 are objected to because of the following informalities: The recitation of PH 75 in claim 58 renders the claim 58 and all dependent claims thereof ambiguous. It is believed the correct recitation should be "7.5" Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 61 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "magnetosomes" is not defined in the specification. Accordingly, the metes and bounds of such language is not clear.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 58-59, 61, 63, 67, 69, 74 are rejected under 35 U.S.C. 102(b) as being anticipated by Unger US Patent 5,770,222.

The instant claims are directed to methods of modifying a therapeutic agent comprising associating the agent with one or more cationic component to produce a composition having optimal range of zeta potential and dispersing the composition in a medium to form colloids having a size of about 10 nm to about 400 nm, wherein the composition exhibits a zeta potential in the range of about +30 mV to +65 mV in about 0.05 mM KCL solution at about pH 7.5.

Unger teaches methods of preparing cationic liposomal therapeutic system comprising a bioactive agent such as taxol (abstract, col 8, lines 25-55; col 49, line 65). The cationic lipids employed by Unger include DOTAP or DOPC which meets the limitations of the instant claim 74. (see col 8, lines 25-29; col 9, lines 24-26; col 36, line 25-col 37, line 67). Unger's particle size range between 30 nm to 5 microns which falls within the instantly described particle sizes (see col 15, lines 5-20). Further, the systems of Unger form a colloidal suspension when placed in an aqueous medium (see col 15, lines 36-67; col 43, line 64-col 46, line 20; col 48, lines 7-10).

Applicant is informed that a prior art composition that comprise all elemental components of the instantly created composition would meet all functional characteristics of the created composition, because such characteristics are inseparable from the composition. Unger meets all elemental steps of the instant claims and the compositions created thereof. Since Unger's compositions was prepared by the same steps as the instantly claimed process and further comprise all elemental components

of the instantly prepared composition, they would inherently exhibit the same zeta potentials and targeting properties as those instantly claimed, because such functional characteristics of the created composition is inseparable from the describe composition of Unger.

Further, the limitation of "magnetosome" in claim 61 is viewed given its broadest reasonable interpretation consistent with the specification. Accordingly, any cationic components that exhibit magnetic properties can fall within the scope of such limitation. Unger discloses and even claims the use of metallic salts and complexes with the cationic lipid moieties either as free radicals generator or as blood products. (col 13, lines 24-55; col 50, lines 7-8). Thus, Unger anticipates such limitation.

Claims 58-59, 63, 67, 69, 74 are rejected under 35 U.S.C. 102(e) as being anticipated by Thierry US Patent 6,110,490.

Thierry teaches methods of preparing drug containing liposomes wherein the specific lipids used in the liposomes are cationic. (see abstract; col 9, lines 5-67; col 30, lines 10-22). Thierry specifically teaches cationic lipids such as DOPE which meets the limitations of claim 74. Thierry's method prepares targeted drug delivery liposomes that can target vascular sites (see col 10, line 45-60; col 11, line 30). The therapeutic agents that are modified by Thierry's method include various cytotoxic drugs such as taxol; which is a taxane compound. (see col 8, line 1-9; col 12, line 13). The therapeutic agents used by Thierry are encapsulated in the liposomes and are suspended in an aqueous medium to form liposomes to having a size in range of 200-

3000nm (see col 25, lines 24-46). Such range of particles falls within the scope of the instantly created particles.

Thierry meets all elemental steps of the instant claims and the compositions created thereof. Since the compositions prepared by Thierry meets all elemental components of the instantly prepared composition, they would inherently exhibit the same zeta potentials as instantly claimed, because such functional characteristics of the

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 60 is rejected under 35 U.S.C. 103(a) as being unpatentable over Thierry or Unger.

The teachings of both Thierry and Unger were described above. They only fails to explicitly state that their employed cationic component complies molecules having an

isoelectric point above 7.5 or that the composition as a whole has an isoelectric point above 7.5.

Nevertheless, since cationic lipids by definition must have a isoelectric point above 7 (see instant specification, pg. 15, at para 0057), absent a showing of unexpected results, it would have been obvious to one of ordinary skill in the art at the time of invention to optimize such parameters during the processes described by either Thierry or Unger by routine experimentations. The ordinary skill in the art would have been motivated to do such optimization to improve stability and delivery of such systems.

Conclusion

No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 571-272-0630. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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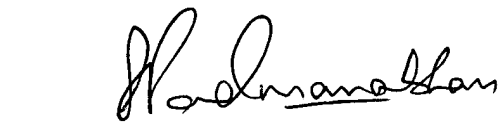

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